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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,976	09/27/2001	David A. Ferrick	A-66038-4/RMS/JJD/DLR	7248

959 7590 01/29/2004

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,976	FERRICK ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on th cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-35* is/are pending in the application.

4a) Of the above claim(s) *30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29 and 31-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/22/2002* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the species of IL-4 inducible promoter in the paper filed 11/03/2003 is acknowledged. The traversal is on the ground(s) that "IL-4 inducible promoter" and "inducible promoter" are not separate species because the IL-4 inducible promoter is a type of inducible promoter. Based on this argument, both the "IL-4 inducible promoter" and "inducible promoter" will be searched. Claims 29, 31-35 read on the elected species and are under consideration. Claim 30 is withdrawn from consideration pursuant to 37 CFR 1.142(b).

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29, 31-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a retroviral vector comprising a fusion nucleic acid comprising: i) an IL-4 inducible epsilon promoter with the sequence as set forth in SEQ ID NO: 1; ii) a first reporter gene; iii) a nucleic acid encoding a 2a site; and iv) a second reporter gene, does not reasonably provide enablement for a retroviral vector comprising a fusion nucleic acid comprising: i) an inducible promoter or an IL-4 inducible epsilon promoter; ii) a first reporter gene; iii) a nucleic acid encoding a 2a site; and iv) a second reporter gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass retroviral vectors comprising inducible promoters or an IL-4 inducible epsilon promoter. The claims as written thus encompass all inducible promoters, while only providing one example, and the term IL-4 inducible promoter is defined in the specification as encompassing derivatives (see page 8, lines 24-25). Applicant only discloses an IL-4 inducible epsilon promoter of SEQ ID NO: 1. Since the claims encompass variant nucleic acids, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims as written do not set forth a functional limitation for which the polynucleotides encompassed by the claims must possess. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polynucleotides, since the skilled artisan would have to first make the polynucleotide variants, but there is no functional limitation set forth for the claimed polynucleotide. Thus, since Applicant has only taught how to test for polynucleotide variants, and has not taught how to make polynucleotide variants, it would require undue experimentation of one of skill in the art to make and use the claimed vectors.

Claims 29, 31-35 are under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims encompass retroviral vectors comprising inducible promoters or an IL-4 inducible epsilon promoter. The claims as written thus encompass all inducible promoters, while only providing one example, and the term IL-4 inducible promoter is defined in the specification as encompassing derivatives (see page 8, lines 24-25). Applicant only discloses an IL-4 inducible epsilon promoter of SEQ ID NO: 1. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of substitutions, deletions, insertions and/or additions that may be made to the promoter. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus

is highly variant, a nucleic acid with a sequence as set forth in SEQ ID NO: 1 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is vague and indefinite in the recitation of the term "2a site". The sequence to which this term refers is not clear from the claim, and the specification does not clearly define it. For example, see page32, line 22-23 which sets forth only that it is a protease cleavage site, but does not give a sequence for it, or even a citation wherein the 2a site is defined. Claims 31-35 are rejected insofar as they depend on the recitation in claim 29 of "2a site".

Claim 34 is vague and indefinite in the recitation of the term "death gene". There is no definition in the claim as to the genes this term encompasses, and the specification (page 10, line 29 to page 11 line 18) provides non-limiting examples of what may be considered a death gene, but no definition is provided.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29, 31, 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Iida et asl. (1996).

Iida et al. (Iida A, Chen ST, Friedmann T, Yee JK. Inducible gene expression by retrovirus-mediated transfer of a modified tetracycline-regulated system. J Virol. 1996 Sep; 70(9): 6054-9) teaches a retroviral vector for delivery of genes into cells (see page 6054, column 2, first paragraph). The retroviral vectors of Iida et al. comprise an inducible promoter of interest (the minimal CMV immediate early gene promoter), a first reporter gene (the CAT gene), a second reporter gene, which is a drug resistance gene (the neoR gene) (see page 6055, Figure 1). The retroviral vector of Iida et al. anticipates all the limitations of the claims, because, as set forth in the rejection under 35 USC 112 second paragraph, supra, the limitation wherein the retroviral vector comprises a 2a sequence is vague and indefinite. Additionally, the encoded proteins would be able to be cleaved by a protease, which is the only indication in the Specification as to the identity of a 2a site, thus it is inherent that the sequences in the vector would encode a protease cleavage site. Thus the sequences in the retroviral vector of Iida et al. meet the all the limitations of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29, 31-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iida et al. (1996) in view of Mikita et al. (1997), further in view of Persons et al. (1997), and further in view of U.S. Patent No. 5,834,266, (Crabtree et al.).

Iida et al. (Iida A, Chen ST, Friedmann T, Yee JK. Inducible gene expression by retrovirus-mediated transfer of a modified tetracycline-regulated system. J Virol. 1996 Sep; 70(9): 6054-9) teaches a retroviral vector for delivery of genes into cells (see page 6054, column 2, first paragraph). The retroviral vectors of Iida et al. comprise an inducible promoter of interest (the minimal CMV immediate early gene promoter), a first reporter gene (the CAT gene), a second reporter gene, which is a drug resistance gene (the neoR gene) (see page 6055, Figure 1).

It is an expected property of the retroviral vectors of Iida et al. that the encoded proteins would be able to be cleaved by a protease, which is the only indication in the Specification as to the identity of a 2a site. Iida et al. does not teach the retroviral vector comprising an IL-4 inducible promoter, a GFP gene, or a death gene.

Mikita et al. teaches that Interleukin-4 (IL-4) stimulation leads to the activation of the signal transducer and activator of transcription 6 (STAT6). Mikita et al. studied the functional properties of STAT6. Mikita et al. cotransfected HEK 293 cells with a reporter construct comprising the IL-4 regulatory element, which is within the immunoglobulin heavy-chain epsilon promoter and expression vectors encoding mutant STAT6 proteins (see page 5815, Figure 4C). Thus Mikita et al. teaches the IL-4 inducible promoter in a vector. Neither Iiida nor Mikita teach a retroviral vector comprising a sequence encoding a fluorescent protein. Persons et al. teaches a retroviral vector comprising the GFP gene . Neither Iida, Mikita nor Persons teach a reporter gene which is a death gene. Crabtree et al. (column 133, claim 210) discloses the use of a genetic construct which is a retroviral vector. Crabtree et al. (column 129, claim 129) further discloses a method of producing a cell which is selectively killed in response to ligand binding, wherein the cell comprises a genetic construct comprising a ligand binding domain, which dimerizes upon ligand binding, and an action domain, which is the intracellular portion of Fas receptor. Also disclosed is the use of another apoptosis inducing genetic construct wherein the action domain comprises the TNF receptor. Thus, it would have been obvious to one of skill in the art at the time the invention was made to make a retroviral vector comprising an IL-4 inducible promoter, a fluorescent protein and a death gene. The motivation and expectation of success is provided in Mikita et al. which teaches the importance of elucidating

the mechanism governing IL-4 induced gene expression (Mikita at 5812, first column, second paragraph), Persons et al. which teaches that GFP can serve as an excellent marker of gene transfer in hematopoietic tissues, and its utilization will allow purification of genetically modified cells ex vivo and the tracking of such cells following transplantation (see Persons et al. at 1785, column 1, fourth paragraph), and Crabtree et al. which discloses that the use of death domain as a reporter is a generally applicable method and can be used for utilizing protein homodimerization, heterodimerization and oligomerization in living cells. The chimeric proteins are designed such that oligomerization triggers cell death as potential in basic investigation of a variety of cellular processes, in regulatably initiating cell death in engineered cells and in regulating the synthesis of proteins of therapeutic or agricultural importance (column 2, lines 32-60).

Conclusion

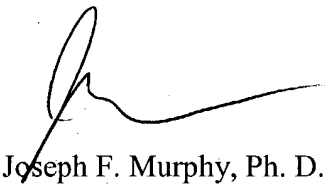
No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
January 22, 2004